

OBSTETRICS

Major dietary patterns and blood pressure patterns during pregnancy: the Generation R Study

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OBJECTIVE: We sought to evaluate associations between dietary patterns and systolic blood pressure (SBP) and diastolic blood pressure during pregnancy.

STUDY DESIGN: This was a prospective study of 3187 pregnant women. Participants completed a food-frequency questionnaire in early pregnancy. The Mediterranean dietary pattern, comprising high intake of vegetables, vegetable oils, pasta, fish, and legumes, and the Traditional dietary pattern, comprising high intake of meat and potatoes, were identified using factor analysis.

RESULTS: A higher SBP was observed among mothers with high Traditional pattern adherence. Low adherence to the Mediterranean pattern

was also associated with higher SBP but only in early and mid pregnancy. A higher diastolic blood pressure throughout pregnancy was observed in mothers with high adherence to the Traditional pattern and low adherence to the Mediterranean pattern. These effect estimates were most pronounced in mid pregnancy.

CONCLUSION: Low adherence to a Mediterranean and high adherence to a Traditional dietary pattern is associated with a higher blood pressure in pregnancy.

Key words: blood pressure, nutrition, observational studies, preeclampsia, pregnancy

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Important maternal cardiovascular changes occur during normal pregnancy including an increase in maternal blood volume that is preceded by vasodilatation, which results in a drop in blood pressure during the first half of gestation, before returning to prepregnancy values toward term.^{1,2} In mothers who develop an elevated blood pressure or preeclampsia, abnormal cardiovascular adaptation occurs reflected by a different pattern of blood pressure change.^{2,3}

Even though the etiology of adverse maternal cardiovascular adaptation to

pregnancy remains unknown, an important role for the endothelium has been suggested.² Various dietary components, such as fatty acids, arginine, vitamin C and E, and folate, have been hypothesized to influence cardiovascular adaptation to pregnancy partly due to their potential effects on endothelial function.⁴

Many dietary factors are correlated and related to other lifestyle factors. Moreover, the single nutrient approach does not take biological complexity resulting from interactions between nutri-

ents into account.⁵ For this reason, recently a shift toward dietary pattern analysis has emerged as a constructive method to explore the relation between diet and disease.

First studies have shown significant associations between dietary patterns and reproductive outcomes.^{6,7} In addition, major dietary patterns, such as a whole grains and fruit dietary pattern or a fats and processed meats dietary pattern, have been associated with biomarker concentrations in the blood that are known to be related to endothelial function, including folate, homocysteine (tHcy), and high-sensitive C-reactive protein (Hs-CRP).^{6,8-10}

From this we hypothesize that dietary patterns may influence maternal cardiovascular adaptation to pregnancy through potential effects on endothelial cell function. We therefore investigated the associations of dietary patterns with biomarker concentrations of endothelial function and maternal blood pressure patterns during pregnancy. Additionally, we focused on the occurrence of gestational hypertension and preeclampsia.

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TABLE 1
Characteristics of 2 dietary patterns

Food group	Correlation coefficient	
	Mediterranean dietary pattern	Traditional dietary pattern
Alcoholic drinks	0.25	0.12
Bread	−0.20	−0.20
Breakfast cereals	0.18	−0.19
Butter	0.07	−0.01
Dairy products	−0.12	0.03
Eggs	0.14	−0.03
Fish	0.43	−0.25
Fruit	0.06	−0.52
Legumes	0.40	−0.00
Margarine	−0.18	0.15
Meat	−0.01	0.74
Nonalcoholic drinks	0.06	−0.30
Pasta, rice	0.68	0.05
Potatoes	−0.03	0.62
Sauces and condiments	−0.09	0.04
Soup	0.16	0.00
Starches and wheat	−0.10	0.01
Sweets	−0.21	−0.12
Vegetable oils	0.70	−0.00
Vegetables	0.76	−0.14

Food group factor loadings for 2 identified dietary patterns from food frequency questionnaire data of 3187 pregnant women in Generation R Study. Factor loadings are presented by Spearman rank correlation coefficients.

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MATERIALS AND METHODS

Study design and cohort

This study was embedded in the Generation R Study, a prospective cohort study that has been previously described in detail.^{11,12} The present study was restricted to prenatally enrolled Dutch women with a live-born singleton, without a medical history of chronic hypertension, diabetes mellitus, hypercholesterolemia, heart disorders, and systemic lupus erythematosus ($n = 3187$).¹³ The study was conducted following the World Medical Association Declaration of Helsinki.¹⁴ Approval was obtained from the Medical Ethics Committee of the Erasmus Medical Center. All participants provided written informed consent.^{11,12}

Nutritional intake

Participants' responses to a self-administered semiquantitative food-frequency questionnaire (FFQ) assessed nutritional intake in the prior 3 months. The questionnaire was administered in early pregnancy (median, 13.5 weeks; interquartile range [IQR], 3.4), and represented a slightly adapted version of the validated FFQ of Klipstein-Grobusch et al.¹⁵ The FFQ consists of 293 items, structured according to meal pattern. Questions include frequency of consumption, portion size, preparation method, and additions. Portion sizes were estimated using Dutch household measures and photographs showing different portion sizes.¹⁶ We calculated average daily nutrient intake by multiplying the frequency of consumption by

portion size and nutrient content per gram based on the 2006 Dutch food composition table.¹⁷

Principal components analysis was used to identify dietary patterns. First the 293 food items were reduced to 20 predefined food groups.¹⁸ Subsequently, food groups were adjusted for total energy intake and principal components analysis was performed to construct overall dietary patterns by explaining the largest proportion of variation in food group intake.¹⁹ The 2 most prevalent factors—from here on referred to as dietary patterns—accounting for 21.5% of the total variation, were selected after rotating the solution using the varimax method.²⁰ The decision to select these 2 factors was based on the criterion that they explained the highest percentage of nutritional intake variance in this study population. In addition, both dietary patterns showed resemblances with earlier reported dietary patterns. This empirical approach resulted in 2 statistically independent dietary patterns (correlation coefficient 0.00), each representing recognizable food consumption patterns in the observed world. The factor loadings, (ie, the associations between the respective dietary patterns and all measured food components) are presented by Spearman rank correlation coefficients (Table 1). Foods with loadings ≥ 0.2 on a factor were used to describe the dietary patterns. The eigenvalue was used to quantify the percentage of variation explained by each dietary pattern. We assigned each participant a personalized score (ie, low adherence, medium adherence, high adherence) for the 2 dietary patterns, representing a quantification of the similarity of the individual's diet with each of the 2 extracted dietary patterns. After computation of these personalized scores, all 3187 women were classified into equal tertiles according to their personal score for the respective dietary patterns.

Blood pressure

Primary outcome variables were maternal blood pressure (mm Hg), gestational hypertension, and preeclampsia. Maternal systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured in early, mid (median, 20.5 weeks; IQR, 1.3), and late (median, 30.4 weeks;

TABLE 2

Selected characteristics stratified into adherence categories of Mediterranean dietary pattern

Variable	Mediterranean dietary pattern			P value
	Low adherence n = 1062	Medium adherence n = 1062	High adherence n = 1063	
Mean maternal age, y	30.2 (4.6)	31.6 (4.0)	32.4 (4.0)	< .01
Median BMI before pregnancy, kg/m ²	23.0 (4.7)	22.1 (3.7)	21.8 (3.5)	< .01
Missing, %	14.1	14.2	12.2	
Median BMI at intake, kg/m ²	24.0 (5.0)	23.0 (4.2)	23.0 (3.6)	< .01
Mean weight gain (delta BMI)	2.8 (1.3)	2.8 (1.2)	2.7 (1.2)	NS
Missing, %	4.2	5.3	4.3	
Obesity at intake (BMI ≥30), %	12.4	6.7	5.3	< .01
Education, %				
Low	5.0	2.7	1.6	< .01
Medium	53.5	32.1	23.3	
High	40.6	64.8	74.7	
Missing	0.9	0.4	0.4	
Parity, %				
0	59.6	59.4	61.1	NS
≥1	40.1	40.5	38.7	
Missing	0.3	0.1	0.2	
Smoking, %				
Yes, still	19.3	13.6	11.5	< .01
Stopped	7.5	7.6	9.5	
No	65.5	70.1	71.8	
Missing	7.7	8.7	7.2	
Folic acid use, %				
No	11.0	7.6	7.6	< .01
Postconception start	24.9	28.8	27.5	
Preconception start	47.7	44.8	47.4	
Missing	16.4	18.8	17.5	
Vomiting, %				
Severe	17.1	12.1	8.7	< .01
Moderate	19.2	19.7	20.5	
No	55.4	59.3	62.9	
Missing	8.3	8.9	7.9	
Mean SBP, mm Hg				
Early pregnancy	118.1 (12.0)	116.8 (11.9)	116.2 (11.4)	< .01
Mid pregnancy	119.5 (11.9)	118.2 (11.8)	117.40 (11.1)	< .01
Late pregnancy	120.76 (11.6)	120.5 (11.6)	119.7 (11.0)	NS

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(continued)

TABLE 2

Selected characteristics stratified into adherence categories of Mediterranean dietary pattern (continued)

Variable	Mediterranean dietary pattern			P value
	Low adherence n = 1062	Medium adherence n = 1062	High adherence n = 1063	
Mean DBP, mm Hg				
Early pregnancy	68.9 (9.3)	67.9 (9.2)	67.5 (8.8)	< .01
Mid pregnancy	68.4 (9.7)	66.6 (9.1)	66.3 (8.7)	< .01
Late pregnancy	69.9 (9.3)	69.1 (9.1)	68.7 (8.9)	< .01
Preeclampsia, %	2.1	1.8	1.6	NS
Gestational hypertension, %	5.6	5.7	4.6	NS

Values represent percentage (%) within column, mean (SD), or median (interquartile range).

Analysis of variance and χ^2 test tested differences in baseline characteristics between Mediterranean dietary pattern categories.

BMI, body mass index; DBP, diastolic blood pressure; NS, not significant; SBP, systolic blood pressure.

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IQR, 1.1) pregnancy using the validated Omron 907 automated digital oscillometric sphygmomanometer (Omron Healthcare Europe BV, Hoofddorp, The Netherlands). The presence of doctor-diagnosed gestational hypertension and preeclampsia was retrieved from medical records and was determined based on the criteria of the International Society for the Study of Hypertension in Pregnancy (Supplement Table 1).^{21,22}

Covariates

Information regarding maternal age, prepregnancy weight, education, parity, smoking, folic acid use, and vomiting was available from questionnaires repeatedly applied during pregnancy. Additionally, at enrollment in early pregnancy, in mid pregnancy, and in late pregnancy, height and weight were measured and body mass index (BMI) (kg/m^2) was calculated.^{11,12} Weight gain is represented as the difference in BMI from early pregnancy until late pregnancy. In early pregnancy venous blood serum and plasma samples were drawn to determine folate, vitamin B12, tHcy, and Hs-CRP concentrations. The between-run coefficients of variation for plasma folate were 8.9% at 5.6 nmol/L, 2.5% at 16.6 nmol/L, and 1.5% at 33.6 nmol/L; the coefficients for serum vitamin B12 were 3.6% at 148 pmol/L, 2.7% at 295 pmol/L, and 3.1% at 590 pmol/L; the coefficients for plasma tHcy were

3.1% at 7.6 $\mu\text{mol}/\text{L}$, 3.1% at 13.7 $\mu\text{mol}/\text{L}$, and 2.1% at 26.1 $\mu\text{mol}/\text{L}$; and the coefficients for plasma Hs-CRP were 0.9% at 12.8 mg/L and 1.3% at 39.3 mg/L.

Statistical analysis

To test differences in baseline characteristics between the dietary pattern categories the analysis of variance and χ^2 test were used. Likewise, trend tests (linear regression) were used to relate the 3 dietary pattern groups to the biomarker concentrations and nutrient intake.

Linear regression was used to assess cross-sectional differences between the dietary pattern categories in DBP and SBP. In the multiple regression analyses the inclusion of confounding variables was based on earlier literature, and determined a priori.^{23,24} These were maternal age, BMI, parity, educational level, smoking, folic acid use, vomiting, and gestational age at time of measurement. In the multiple regression analyses, missing covariables were completed using multiple imputation (missing: BMI 0.4%, educational level 0.6%, parity 0.2%, smoking 7.5%, folic acid use 17.5%, and vomiting 8.3%). Data were imputed according to the Markov Chain Monte Carlo method assuming no monotone missing pattern. Five imputed datasets were created. Subsequently, multiple regression analyses were performed on each imputed dataset

and thereafter combined to 1 pooled estimate.²⁵

To further explore blood pressure trajectories between the dietary pattern categories repeated measurement regression models were used with maternal blood pressure as repeated outcome measure. These models take the correlation between repeated measurements of the same subject into account. The best fitting models were constructed using fractional polynomials of gestational age (Supplement Table 2).²⁶

Lastly, to analyze the associations of the dietary patterns with gestational hypertension and preeclampsia, simple and multiple logistic regression models were used.

We performed all statistical analyses using the Statistical Package of Social Sciences release 17.0 for Windows (SPSS Inc, Chicago, IL), the Statistical Analysis System version 9.2 (SAS Institute Inc, Cary NC), and R version 2.9.2 for Windows.

RESULTS

Characteristics on nutritional intake of the 3187 women are shown in Table 1. The first factor explained 12.8% of nutritional intake total variance and was labeled the Mediterranean dietary pattern. It comprised high intake of vegetables, vegetable oils, pasta, rice, fish, and legumes, moderate intake of alcohol, and low intake of sweets. The second factor

explained 8.7% of nutritional intake total variance. It was labeled the Traditional dietary pattern as it was characterized by high intake of meat and potatoes, and low intake of fruit, nonalcoholic drinks, fish, and bread. Maternal characteristics associated with both low adherence to the Mediterranean dietary pattern and high adherence to the Traditional dietary pattern were younger age, higher BMI, lower educational level, continued smoking during pregnancy, a lower frequency of folic acid use, and more vomiting (Tables 2 and 3).

Compared to women with high adherence to the Mediterranean dietary pattern, lower plasma folate ($P < .01$) and serum vitamin B12 concentrations ($P < .01$), and higher plasma Hs-CRP concentrations ($P < .01$) were observed among women with low adherence (Table 4). They also had a lower ratio of unsaturated to saturated fatty acid intake, relatively lower intake of protein and fiber, and higher intake of carbohydrates. Women with high adherence to the Traditional dietary pattern had lower plasma folate concentrations ($P < .01$), but higher serum vitamin B12 concentrations ($P < .01$), as compared to women with low adherence to the Traditional dietary pattern. They had higher plasma tHcy ($P < .01$) and Hs-CRP concentrations ($P < .05$), a higher proportion of energy derived from fat, and a lower ratio of unsaturated to saturated fats. These women also consumed relatively lower amounts of vegetable protein, carbohydrates, and fiber.

A consistently higher SBP was observed throughout pregnancy among mothers with high adherence to the Traditional dietary pattern (Table 5). As compared to low adherence, high adherence was associated with a 1.8 mm Hg (95% confidence interval [CI], 0.7–2.9) increase in SBP in early pregnancy, a 2.3 mm Hg (95% CI, 1.2–3.3) increase in mid pregnancy, and a 2.6 mm Hg (95% CI, 1.6–3.6) increase in late pregnancy. Low adherence to the Mediterranean dietary pattern was associated with comparable effects in early and mid pregnancy (differences: 1.1 mm Hg; 95% CI, 0.2–2.2 and 1.3 mm Hg; 95% CI, 0.3–2.3, respectively). This trend disappeared in

TABLE 3

Selected characteristics stratified into adherence categories of Traditional dietary pattern

Variable	Traditional dietary pattern			P value
	Low adherence n = 1062	Medium adherence n = 1063	High adherence n = 1062	
Mean maternal age, y	32.0 (3.9)	31.5 (4.2)	30.7 (4.8)	< .01
Median BMI before pregnancy, kg/m ²	21.9 (3.7)	22.3 (3.7)	22.7 (4.6)	< .01
Missing, %	12.9	14.2	13.2	
Median BMI at intake, kg/m ²	22.8 (3.8)	23.3 (4.1)	23.8 (5.1)	< .01
Mean weight gain (delta BMI)	2.8 (1.2)	2.8 (1.2)	2.7 (1.2)	NS
Missing, %	3.7	4.3	5.6	
Education, %				
Low	0.7	3.4	5.3	< .01
Medium	26.4	33.7	48.9	
High	72.3	62.3	45.5	
Missing	0.6	0.6	0.3	
Parity, %				
0	69.4	58.9	52.0	< .01
≥1	30.4	41.0	47.9	
Missing	0.2	0.1	0.1	
Smoking, %				
Yes, still	7.5	14.2	22.6	< .01
Stopped	7.5	9.0	8.1	
No	76.5	68.0	62.9	
Missing	8.5	8.8	6.4	
Folic acid use, %				
No	5.7	7.7	12.8	< .01
Postconception start	27.1	24.6	29.4	
Preconception start	51.9	48.2	40.3	
Missing	15.3	19.5	17.5	
Vomiting, %				
Severe	12.0	12.3	13.6	< .01
Moderate	18.0	19.8	21.5	
No	62.0	58.2	57.8	
Missing	8.0	9.7	7.1	
Mean SBP, mm Hg				
Early pregnancy	116.1 (11.5)	117.0 (11.8)	118.0 (12.0)	< .01
Mid pregnancy	117.0 (11.1)	118.5 (11.3)	119.6 (12.3)	< .01
Late pregnancy	119.1 (10.9)	119.8 (11.1)	122.0 (12.0)	< .01
Mean DBP, mm Hg				
Early pregnancy	67.6 (8.9)	68.2 (9.1)	68.5 (9.3)	NS
Mid pregnancy	66.4 (9.1)	67.3 (9.2)	67.6 (9.4)	< .01
Late pregnancy	69.0 (9.1)	69.1 (8.8)	69.9 (9.5)	NS
Preeclampsia, %	1.8	1.3	2.4	NS
Gestational hypertension, %	5.0	5.0	5.9	NS

Values represent percentage (%) within column, mean (SD), or median (interquartile range).

Analysis of variance and χ^2 test tested differences in baseline characteristics between Traditional dietary pattern categories.

BMI, body mass index; DBP, diastolic blood pressure; NS, not significant; SBP, systolic blood pressure.

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TABLE 4

Biomarker concentrations and nutrient intake stratified into adherence categories of 2 dietary patterns

Variable	Mediterranean dietary pattern						Traditional dietary pattern					
	Low adherence		Medium adherence		High adherence		Low adherence		Medium adherence		High adherence	
	n = 1062		n = 1062		n = 1063		n = 1062		n = 1063		n = 1062	
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR
Biomarker concentrations												
Folate, nmol/L	18.3	13.9	19.2	13.4	19.9	12.6	21.0	12.8	19.3	13.3	16.9	13.7
tHcy, μ mol/L	7.0	2.1	7.0	1.9	7.0	1.8	7.0	1.8	6.9	2.0	7.1	2.1
Vitamin B12, pmol/L	167.0	99.0	178.0	99.0	182.0	96.3	174.0	90.0	173.0	100.0	180.0	111.5
Hs-CRP, mg/L	4.6	5.7	4.0	5.4	3.8	4.5	3.4	4.9	4.1	5.0	4.7	5.7
Energy and macronutrients												
Energy, kJ/d	8955.9	3245.2	8914.3	2967.2	8993.2	2815.5	9018.9	3008.5	8887.9	2896.3	9107.8	3113.5
Fat, % of energy	35.9	7.7	36.7	7.0	36.8	6.8	34.9	7.7	36.8	6.6	37.6	7.1
Total fat, g/d	77.7	16.5	79.5	15.2	79.9	14.8	75.6	16.6	79.7	14.2	81.6	15.6
Saturated lipids, g/d	29.0	6.9	28.9	6.7	28.6	6.6	27.2	6.6	29.1	6.5	30.2	6.3
Monounsaturated lipids, g/d	27.0	6.4	28.4	6.2	29.9	6.9	27.3	7.0	28.4	6.1	29.5	6.8
Polyunsaturated lipids, g/d	17.9	7.0	18.3	6.3	17.9	6.4	17.8	6.6	18.2	6.3	18.2	6.9
Unsaturated/saturated lipids	1.9	0.4	2.0	0.4	2.1	0.4	2.0	0.5	1.9	0.4	1.9	0.4
Protein, % of energy	14.1	3.1	15.0	2.7	15.3	2.9	15.6	2.9	14.9	2.9	15.0	3.0
Total protein, g/d	69.6	14.9	74.0	12.9	75.7	13.5	72.0	13.7	73.0	13.4	74.5	14.7
Vegetable protein, g/d	26.0	7.0	28.4	6.4	29.6	6.4	30.7	6.4	28.0	5.7	25.6	6.4
Animal protein, g/d	43.1	15.0	45.1	13.9	45.9	14.9	40.9	14.1	44.9	13.5	48.0	14.3
Carbohydrate, % of energy	49.7	9.0	48.3	7.5	47.0	7.5	50.1	8.3	48.0	7.4	46.8	7.9
Total carbohydrate, g/d	241.8	43.6	234.3	37.0	228.4	37.1	243.7	40.6	233.3	37.3	227.4	38.8
Carbohydrates monosaccharides, g/d	138.8	46.2	127.6	37.9	117.3	35.3	135.0	40.8	126.0	38.7	120.8	42.6
Carbohydrates polymers, g/d	100.0	22.5	104.8	22.5	108.7	25.0	104.9	22.2	105.1	23.0	103.8	25.5
Fiber, g/d	19.3	5.7	21.7	5.6	23.5	6.1	24.0	6.3	21.2	5.4	19.4	5.9

Hs-CRP, high-sensitive C-reactive protein; IQR, interquartile range; tHcy, homocysteine.

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late pregnancy (difference: 0.2 mm Hg; 95% CI, -0.8 to 1.2). Higher DBP readings were observed during pregnancy in mothers with both high adherence to the Traditional dietary pattern and low adherence to the Mediterranean dietary pattern. These increases were most pronounced during the mid pregnancy period (differences: 1.3 mm Hg; 95% CI, 0.5–2.1 and 1.6 mm Hg; 95% CI, 0.8–2.4, respectively, for high adherence to the Traditional, and low adherence to the Mediterranean dietary pattern).

Repeated regression analyses showed similar trends in patterns of blood pressure change. Overall, SBP and DBP were

highest among women with low adherence to the Mediterranean dietary pattern (Figure 1) and high adherence to the Traditional dietary pattern (Figure 2).

Neither adherence to the Mediterranean dietary pattern nor adherence to the Traditional dietary pattern was associated with the occurrence of gestational hypertension or preeclampsia (Table 6).

COMMENT

We showed that adherence to 2 independent dietary patterns, respectively, low adherence to a Mediterranean dietary pattern and high adherence to a Traditional dietary pattern, is associated with a

higher maternal blood pressure during pregnancy. These associations are within physiologic ranges. We observed no relation with the occurrence of hypertensive pregnancy disorders.

During recent years, the Mediterranean dietary pattern has gained considerable attention for its positive health effects.²⁷ There is no single Mediterranean diet, although dietary patterns prevailing in the Mediterranean region share common characteristics including an abundance of vegetables, vegetable oil as principal source of fat, moderate amounts of fish and poultry, relatively low consump-

TABLE 5

Associations between dietary patterns and maternal blood pressure in early, mid, and late pregnancy

Variable	SBP early pregnancy		SBP mid pregnancy		SBP late pregnancy	
	Crude ^a	Adjusted ^b	Crude ^a	Adjusted ^b	Crude ^a	Adjusted ^b
Mediterranean dietary pattern						
Low adherence	1.8 [0.7–2.9]	1.1 [0.2–2.2]	2.2 [1.2–3.2]	1.3 [0.3–2.3]	1.0 [0.1–2.0]	0.2 [–0.8 to 1.2]
Medium adherence	0.5 [–0.6 to 1.6]	0.4 [–0.7 to 1.5]	0.8 [–0.2 to 1.8]	0.7 [–0.3 to 1.6]	0.8 [–0.2 to 1.8]	0.7 [–0.3 to 1.6]
High adherence	Reference	Reference	Reference	Reference	Reference	Reference
Trend score	–0.7 [–1.2 to –0.3]	–0.4 [–0.9 to –0.1]	–0.9 [–1.3 to –0.5]	–0.5 [–0.9 to –0.1]	–0.4 [–0.8 to –0.1]	–0.1 [–0.5 to 0.1]
Traditional dietary pattern						
Low adherence	Reference	Reference	Reference	Reference	Reference	Reference
Medium adherence	0.8 [–0.3 to 1.9]	0.8 [–0.2 to 1.9]	1.4 [0.4–2.4]	1.3 [0.4–2.3]	0.7 [–0.3 to 1.7]	0.7 [–0.3 to 1.6]
High adherence	1.9 [0.8–3.0]	1.8 [0.7–2.9]	2.5 [1.5–3.5]	2.3 [1.2–3.3]	2.9 [2.0–3.9]	2.6 [1.6–3.6]
Trend score	0.6 [0.1–1.0]	0.5 [0.1–1.0]	0.9 [0.5–1.3]	0.8 [0.4–1.3]	1.0 [0.6–1.5]	0.9 [0.5–1.3]
	DBP early pregnancy		DBP mid pregnancy		DBP late pregnancy	
	Crude ^a	Adjusted ^b	Crude ^a	Adjusted ^b	Crude ^a	Adjusted ^b
Mediterranean dietary pattern						
Low adherence	1.3 [0.5–2.1]	0.9 [0.1–1.8]	2.2 [1.2–3.2]	1.6 [0.8–2.4]	1.4 [0.6–2.2]	1.0 [0.2–1.8]
Medium adherence	0.3 [–0.6 to 1.1]	0.3 [–0.6 to 1.1]	0.8 [–0.2 to 1.8]	0.2 [–0.6 to 0.9]	0.5 [–0.3 to 1.3]	0.5 [–0.3 to 1.2]
High adherence	Reference	Reference	Reference	Reference	Reference	Reference
Trend score	–0.4 [–0.8 to –0.1]	–0.3 [–0.6 to –0.1]	–0.8 [–1.2 to –0.5]	–0.6 [–1.0 to –0.3]	–0.5 [–0.8 to –0.2]	–0.3 [–0.7 to –0.1]
Traditional dietary pattern						
Low adherence	Reference	Reference	Reference	Reference	Reference	Reference
Medium adherence	0.5 [–0.4 to 1.3]	0.6 [–0.3 to 1.4]	0.1 [–0.6 to 0.8]	0.9 [0.1–1.7]	–0.2 [–0.9 to 0.5]	0.3 [–0.4 to 1.1]
High adherence	0.9 [0.1–1.7]	1.0 [0.1–1.8]	1.9 [1.3–2.0]	1.3 [0.5–2.1]	1.1 [0.5–1.8]	0.8 [0.1–1.6]
Trend score	0.4 [0.0–0.7]	0.4 [0.1–0.8]	0.5 [0.2–0.8]	0.6 [0.2–0.9]	0.2 [–0.2 to 0.5]	0.3 [–0.1 to 0.6]

Results from cross-sectional linear regression analyses. Values are regression coefficients (95% confidence interval) and reflect differences in SBP and DBP (mm Hg) compared to reference, in early (2706 measurements), mid (3125 measurements), and late (3108 measurements) pregnancy.

DBP, diastolic blood pressure; SBP, systolic blood pressure.

^a Crude: adjusted for gestational age at measurement; ^b Adjusted: additionally adjusted for maternal age, body mass index, parity, educational level, smoking, vomiting, and folic acid use.

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tions of meat, and moderate alcohol use.^{27,28} Adherence to the identified Mediterranean dietary pattern in our study was validated by higher amounts of vegetable protein, carbohydrates polymers, fiber, and a favorable ratio of unsaturated to saturated lipids. Increased concentrations of the biomarkers plasma folate and serum vitamin B12 further validated adherence to the Mediterranean dietary pattern.

The Traditional dietary pattern resembles a typically Northwest European di-

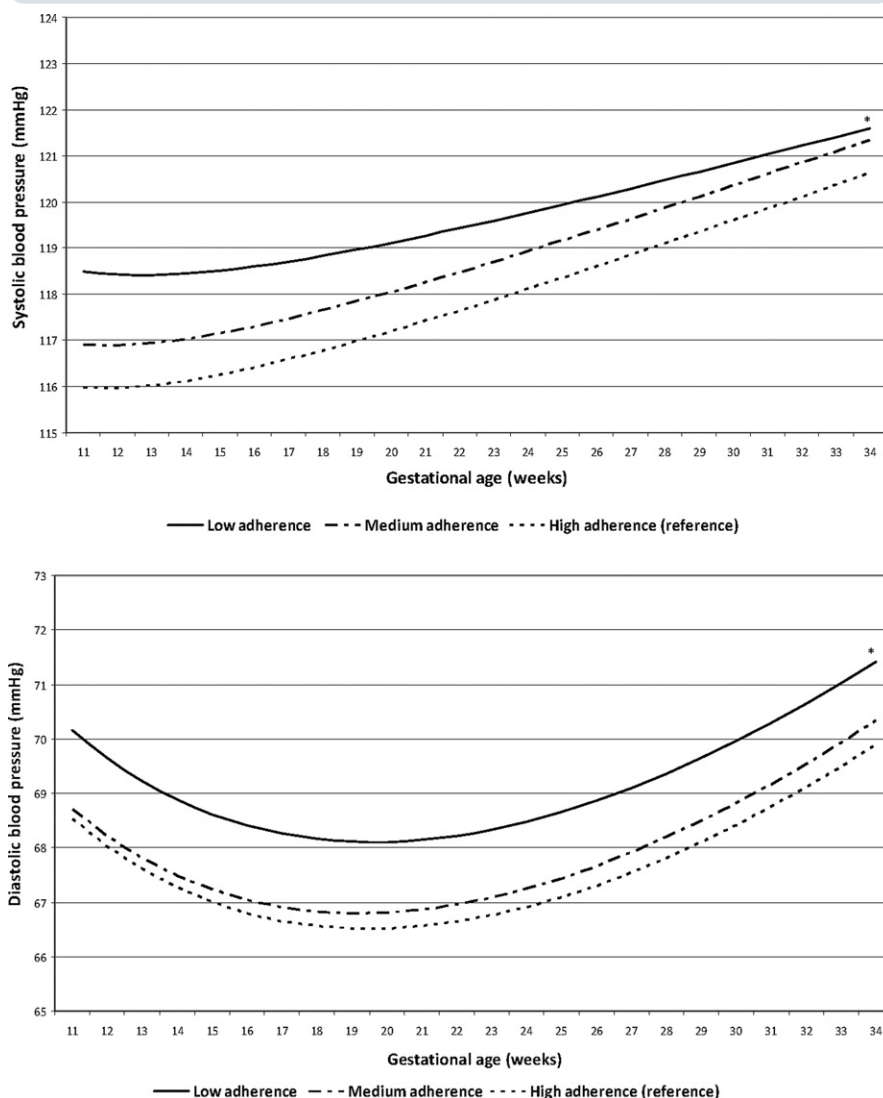
etary tradition that has existed since the 19th century when agriculture and domestic education were widely implemented. Characterized by high amounts of meat and potatoes, the Traditional dietary pattern seems fairly reproducible across populations.²⁸ In our study adherence to this dietary pattern was validated by higher amounts of animal protein and saturated lipids, lower amounts of carbohydrates and fiber, lower concentrations of plasma folate,

and higher concentrations of serum vitamin B12.

Our group is the first to find associations between dietary patterns in an ethnic homogenous group of pregnant women and the course of blood pressure during pregnancy. Even though baseline nonpregnant blood pressure levels were not measured as women were only included in the Generation R Study from early pregnancy onward, the observed higher blood pressure levels in early

FIGURE 1

Blood pressure patterns in Mediterranean dietary pattern categories



Change in systolic blood pressure (SBP) and diastolic blood pressure (DBP) in mm Hg per Mediterranean dietary pattern category with high adherence as reference group based on repeated measurement analysis ($SBP = \beta_0 + \beta_1 * \text{dietary pattern} + \beta_2 * GA + \beta_3 * GA^{-2} + \beta_4 * \text{dietary pattern} * GA$. $DBP = \beta_0 + \beta_1 * \text{dietary pattern} + \beta_2 * GA + \beta_3 * GA^{-5} + \beta_4 * \text{dietary pattern} * GA$) ($n = 3187$).

GA, gestational age in weeks.

* $P < .05$ reflects significant difference in change in blood pressure per week (β_4) per Mediterranean dietary pattern category, for different categories compared to reference.

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pregnancy, for women with either low adherence to the Mediterranean dietary pattern, or high adherence to the Traditional dietary pattern, may indicate that blood pressure was already higher before pregnancy. This finding is in line with that of others. In the past, it was suggested in a review on metabolic studies, prospective cohort studies, and clinical trials, that the use of dietary patterns rich

in whole grains, fruit, vegetables, and adequate omega-3 fatty acids, and low in refined grains, and saturated and trans fats, protected against cardiovascular disease.²⁹ Indeed, it has been demonstrated that such a diet lowered SBP and DBP levels by 5.5 and 3.0 mm Hg in adults with SBP of <160 mm Hg and DBP readings of 80–95 mm Hg.³⁰ Additionally, van Dam et al³¹ reported on 2

dietary patterns that were associated with SBP levels in Dutch nonpregnant women aged 20–65 years. These included a blood pressure–lowering diet characterized by higher intake of vegetables, rice, chicken, fish, and wine, and a blood pressure–elevating diet, characterized by greater intake of meat and potatoes, and lesser intake of low-fat dairy products and fruit.³¹

To our knowledge, the additional observed different patterns of blood pressure change during pregnancy have not been observed before. Higher SBP and DBP were observed in mothers with both low adherence to the Mediterranean dietary pattern and high adherence to the Traditional dietary pattern. However, this difference declined with gestational age in women with low adherence to the Mediterranean dietary pattern. With respect to DBP, the differences were most pronounced in mid pregnancy. These observed blood pressure patterns might be explained by effects of the dietary patterns on endothelial cell function, possibly interfering with normal vascular adjustments (vasodilatation) to pregnancy.²³ Differential effects on the amount of oxidative stress and thereby endothelial cell functions from antioxidant vitamins, omega-3 fatty acids, magnesium, fiber, and folic acid may underlie these biological processes. In this respect, dietary patterns have been demonstrated to reduce markers of inflammation and endothelial dysfunction, similar to our results on Hs-CRP concentrations.⁹ This may imply that the first trimester is a critical period for cardiovascular adaptations related to maternal nutrition and subsequent blood pressure development.³² Interestingly, our results are different from our previous findings on the association between synthetic folic acid and blood pressure, showing a small physiological increase in maternal blood pressure among folic acid–supplemented women.⁸ This might be explained by the stronger and opposite effects of other nutritional compounds than folate. Moreover, in contrast to food folate, folic acid appears also in an oxidized form in the blood that may slightly increase blood pressure by a differential effect on endothelium function.³³ Lastly, concerning the Traditional dietary pattern, it can be hy-

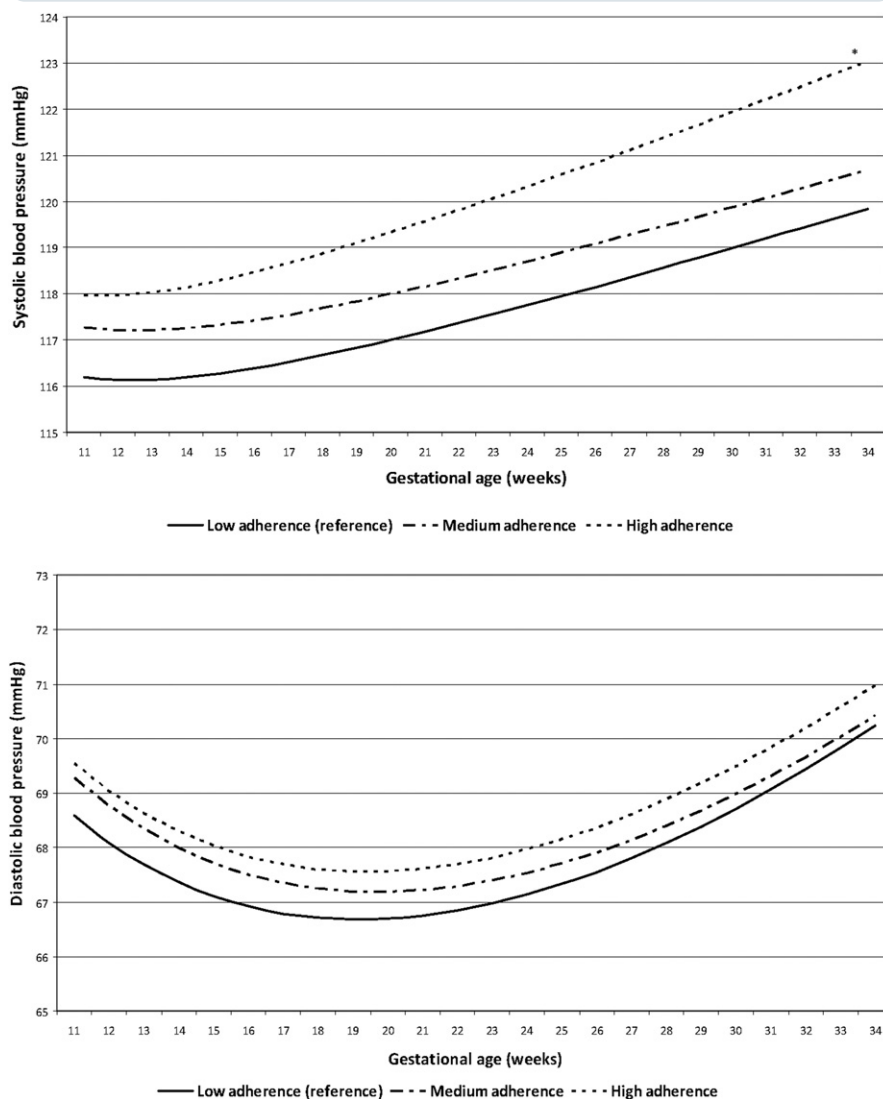
pothesized that the lower consumption of fluids in women with high adherence affected the relative state of hypovolemia associated with early pregnancy with subsequent differential hemodynamic adaptation. Future studies are needed to elucidate on these effects and potential mechanisms.

Despite an elevated blood pressure throughout pregnancy and a relatively less steep midpregnancy fall in DBP we observed no associations with the risks of gestational hypertension or preeclampsia. Thus, the effects of these dietary patterns may not be strong enough to be associated with the risk of hypertensive pregnancy disorders. Recently, Brantsaeter et al³⁴ found that a dietary pattern characterized by high intake of vegetables and vegetable oils decreased the risk of preeclampsia, whereas a dietary pattern characterized by a high consumption of meat, sweet drinks, and snacks increased the risk. These results are in disparity with our study. In their study lack of validation of the diagnosis preeclampsia might have influenced the results. As we were limited by a relatively small number of preeclamptic cases in this restricted study sample, further larger studies with more power are needed.

Dietary pattern analysis is complementary to approaches using individual foods or nutrients that are limited by biologic interactions and collinearity.⁵ The large sample size of this study together with its prospective design enabled us to assess associations between maternal dietary patterns and blood pressure in close detail. However, our results should be considered in light of some potential limitations. First, nutritional intake was assessed in early pregnancy. It could be argued that nutritional intake differs between different pregnancy periods. However, Cucó et al³⁵ investigated dietary patterns during different pregnancy periods and observed no significant differences over time. Moreover, we assessed diet before occurrence of the outcome which implies that potential misclassification would likely have been nondifferential. An important issue is unmeasured confounding. We addressed this by restricting to an ethnic homogeneous population and by controlling for a large number of confounders, including the important covariates maternal weight and socioeconomic class. Even though these and

FIGURE 2

Blood pressure patterns in Traditional dietary pattern categories



Change in systolic blood pressure (SBP) and diastolic blood pressure (DBP) in mm Hg per Traditional dietary pattern category with low adherence as reference group based on repeated measurement analysis. (SBP = $\beta_0 + \beta_1 * \text{dietary pattern} + \beta_2 * \text{GA} + \beta_3 * \text{GA}^{-2} + \beta_4 * \text{dietary pattern} * \text{GA}$. DBP = $\beta_0 + \beta_1 * \text{dietary pattern} + \beta_2 * \text{GA} + \beta_3 * \text{GA}^{-5} + \beta_4 * \text{dietary pattern} * \text{GA}$) (n = 3187).

GA, gestational age in weeks.

* $P < .05$ reflects significant difference in change in blood pressure per week (β_4) per Traditional dietary pattern category, for different categories compared to reference.

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other used covariates are strongly related to other health-related behaviors and maternal blood pressure, residual confounding cannot be excluded completely. Lastly, assuming our missing data were missing at random we used multiple imputation to deal with missing values since this method is currently believed to be the most credible.³⁶

The major challenge in dietary pattern analysis remains to establish a quantitative method to identify eating patterns unless a specific pattern has been specified before. Using factor analysis involves several arbitrary decisions including the consolidation of food items into food groups, the number of factors to extract, rotation method, and factor label-

TABLE 6

Associations between dietary patterns and hypertensive pregnancy disorders

Variable	Gestational hypertension			Preeclampsia		
	n cases	Crude ^a	Adjusted ^b	n cases	Crude ^a	Adjusted ^b
Mediterranean dietary pattern						
Low adherence	58	1.2 [0.8–1.7]	1.3 [0.9–1.9]	22	1.3 [0.6–2.3]	1.2 [0.6–2.3]
Medium adherence	59	1.2 [0.8–1.8]	1.1 [0.8–1.7]	19	1.2 [0.7–2.4]	1.2 [0.6–2.3]
High adherence	48	Reference	Reference	17	Reference	Reference
Trend score		0.9 [0.8–1.0]	0.9 [0.8–1.1]		0.9 [0.7–1.2]	0.8 [0.6–1.1]
Traditional dietary pattern						
Low adherence	52	Reference	Reference	19	Reference	Reference
Medium adherence	52	0.9 [0.7–1.5]	1.0 [0.7–1.6]	14	0.7 [0.3–1.4]	0.7 [0.3–1.4]
High adherence	61	1.2 [0.8–1.7]	1.3 [0.9–1.9]	25	1.2 [0.6–2.2]	1.1 [0.6–2.1]
Trend score		1.1 [0.9–1.2]	1.1 [0.9–1.3]		1.1 [0.8–1.4]	1.3 [0.9–1.7]

Results from logistic regression analysis. Values are odds ratios (95% confidence interval).

^a Unadjusted; ^b Adjusted for maternal age, body mass index, parity, educational level, smoking, vomiting, and folic acid use.

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ing.³⁷ We conducted sensitivity analyses to examine whether these decisions affected our results. The use of other types of factor analysis (oblique instead of orthogonal rotation) and analyses within a random subgroup (25%) indicated that the identified patterns were robust. Also, the addition or deletion of 1 or 2 food groups did not have much effect on the general pattern of findings. Moreover, similar dietary patterns derived by factor analysis have been observed by others.^{7,28,31,34}

Concluding from our results, both low adherence to a Mediterranean dietary pattern and high adherence to a Traditional dietary pattern are independently associated with physiological higher levels of blood pressure. The differential effects with respect to the patterns of blood pressure change should be further explored. ■

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SUPPLEMENTARY TABLE 1

Applied criteria for diagnosis of gestational hypertension and preeclampsia

Criteria gestational hypertension

New-onset hypertension

(ie, SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg >20 wk' gestation in previously normotensive woman on at least 2 occasions)

Criteria preeclampsia

(1) New-onset hypertension

(ie, SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg >20 wk' gestation in previously normotensive woman on at least 2 occasions) and

(2) proteinuria

(ie, ≥ 2 dipstick readings of $\geq 2+$, 1 sample reading of $\geq 1+$, or 24-hour urine collection containing at least 300 mg of protein)

DBP, diastolic blood pressure; SBP, systolic blood pressure.

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SUPPLEMENTARY TABLE 2

Estimates of intercept and interaction terms of dietary pattern with fractional polynomials for maternal blood pressure

Mediterranean dietary pattern	Intercept		Fractional polynomials	
	Crude	Adjusted	GA crude	GA adjusted
SBP				
Low adherence	3.2609 [1.6945-4.8272]	2.3736 [0.8135-3.9337]	-0.0675 [-0.128 to -0.007]	-0.0661 [-0.127 to -0.005]
Medium adherence	1.0381 [-0.5234 to 2.5995]	0.8920 [-0.6535 to 2.4375]	-0.0094 [-0.069 to 0.051]	-0.0098 [-0.070 to 0.051]
High adherence	Reference	High adherence	Reference	Reference
DBP				
Low adherence	1.6852 [0.4734-2.8970]	1.2604 [0.05642-2.4644]	-0.0048 [-0.051 to 0.042]	-0.0040 [-0.005 to 0.042]
Medium adherence	0.0473 [-1.1604 to 1.2552]	0.00313 [-1.1607 to 1.223]	0.0119 [-0.034 to 0.058]	0.0115 [-0.035 to 0.058]
High adherence	Reference	High adherence	Reference	Reference
Traditional dietary pattern	Intercept		Fractional polynomials	
	Crude	Adjusted	GA crude	GA adjusted
SBP				
Low adherence	Reference	Reference	Reference	Reference
Medium adherence	1.2049 [-0.3479 to 2.7577]	1.1571 [-0.3824 to 2.6966]	-0.0105 [-0.071 to 0.049]	-0.0110 [-0.071 to 0.049]
High adherence	1.0839 [-0.4730 to 2.6408]	0.8407 [-0.7155 to 2.3970]	0.0622 [0.002-0.123]	0.061 [0.001-0.122]
DBP				
Low adherence	Reference	Reference	Reference	Reference
Medium adherence	0.9465 [-0.2570 to 2.1500]	1.0614 [-0.1280 to 2.2508]	-0.0227 [-0.069 to 0.024]	-0.0228 [-0.069 to 0.023]
High adherence	1.0623 [-0.1443 to 2.2689]	1.1884 [-0.0144 to 2.9313]	-0.0094 [-0.056 to 0.037]	-0.0104 [-0.057 to 0.036]

Results from repeated measurement models: (1) SBP = $\beta_0 + \beta_1$ * dietary pattern + β_2 * GA + β_3 * GA⁻² + β_4 * dietary pattern * GA. (2) DBP = $\beta_0 + \beta_1$ * dietary pattern + β_2 * GA + β_3 * GA⁻⁵ + β_4 * dietary pattern * GA. Term " $\beta_0 + \beta_1$ * dietary pattern" reflects intercept, and " β_2 * GA + β_3 * GA⁻²" reflects slope of change in blood pressure per week for SBP. " β_2 * GA + β_3 * GA⁻⁵" reflects slope of change in blood pressure per week for DBP. Term " β_4 * dietary pattern * GA" reflects difference in change in blood pressure per week between different dietary pattern categories for SBP and DBP. SBP and DBP effect estimates in mm Hg. Adjusted models are adjusted for maternal body mass index, maternal age, parity, educational level, smoking, vomiting, and periconception folic acid use.

DBP, diastolic blood pressure; GA, gestational age in weeks; SBP, systolic blood pressure.

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